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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,350	03/12/2004	Valery Krasnoperov	VASG-P01-002	2293

28120 7590 02/14/2006

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EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/800,350	KRASNOPEROV ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *1-25 and 35-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The Election filed 1/9/06 in response to the Office Action of 10/6/05 is acknowledged and has been entered. Applicant elected group III, drawn to an antagonist antibody which binds to an extracellular domain of an EphB4 protein and inhibits an activity of EphB4, with traverse.

The traversal is on the ground(s) that Applicant alleges that the Examiner has not shown that there would be a serious burden in examining the Groups set forth in the restriction requirement. In particular, Applicants state: "...it appears that the search for Groups III and VII would be co-extensive. It appears that a search covering the subject matter of Group III would cover the subject matter of Group VII as well since these two groups encompass overlapping subject matter; that is, a antagonist anti-EphB4 antibodies and methods of using same. Thus, Applicants respectfully submit that the invention of Groups III and VII can be efficiently searched and examined together without placing a significant additional burden on the Examiner." This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in the Office Action. Further, it is noted that the Office Action of 10/6/05 indicated that although inventions III and VII are related as product and process of use, the inventions were described as being distinct since the products of group III can be used in a materially different process than that of group VII (see MPEP 806.05(h)). Further, searching and examining the products of group III with the

methods of group VII would result in a serious burden on the examiner since different searches and patentability issues are involved in the examination of these groups. Furthermore, it is noted that the literature search, particularly relevant in this art, is not coextensive and is very important in evaluating the burden of search. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

As indicted in the Office Action of 10/6/05, the originally presented claims had been misnumbered. The Examiner has renumbered the claims in accordance with 37 CFR 1.126. Renumbering of the claims began with the second "23", which was renumbered "24". Subsequent claims have been renumbered 25-62.

Claims 1-62 are pending.

Claims 1-25 and 35-62 are withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claims 26-34 are currently under consideration.

Specification

The specification is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page 19). Applicant is required to delete all embedded hyperlinks and/or other form of browser-executable codes. See MPEP § 608.01.

The specification is objected to on pages 46, 55, 64, 71, 72, 77, 81, 82, 89, 92, 93, and 95-102 for improper disclosure of polynucleotide sequences, as it fails to comply with the requirements of 37 CFR 1.821 through 1.825. This definition sets forth limits, in terms of numbers of amino acids and/or numbers of nucleotides, at or above which compliance with the sequence rules is required. Nucleotide and/or amino acid sequences as used in 37 CFR 1.821 through 1.825 are interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides. (see MPEP 2422). Proper correction is required.

Claim Objections

Claims 26-34 are objected to for being drawn to an unelected invention. The unelected invention, which is part of group IV, is recited in claim 26 (b): "an antibody which binds to an extracellular domain of an Ephrin B2 protein and inhibits an activity of the Ephrin B2." Further, claims 28 and 29 provide limitations to the unelected inventions, as they recite that the unelected antibody "inhibits clustering of Ephrin B2" and "inhibits phosphorylation of Ephrin B2". Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 26-34 rejected under 35 U.S.C. 101 because claim 26, as written, does not sufficiently distinguish over antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Stephenson et al (BMC Molecular Biology, 12/21/01, 2(15): 1-9) or Inada et al (Blood, 1997, 89(8): 2757-2765) as further evidenced by Santa Cruz Biotechnology Inc datasheet for EphB4 (H-200).

The claims are drawn to antibodies which bind to an extracellular domain of an EphB4 protein and inhibit an activity of EphB4. The claims are further drawn to

antibodies which bind to an extracellular domain of an EphB4 protein and inhibit interactions between Ephrin B2 and EphB4 and antibodies which bind to an extracellular domain of an EphB4 protein and inhibit phosphorylation of EphB4. The claims are further drawn to compositions and kits comprising the above antibodies and pharmaceutically acceptable carriers. The claims are further drawn to the above antibodies being monoclonal or polyclonal.

Stephenson et al teaches a polyclonal antibody kit available from Santa Cruz Biotechnology Inc (page 8 left column), EphB4 (H-200). As evidenced by Santa Cruz Biotechnology Inc datasheet for EphB4 (H-200), EphB4 (H-200) was raised against amino acids 201-400 mapping within the extracellular domain of human EphB4. Further, it is noted that the Santa Cruz Inc datasheet for EphB4 (H-200) teaches that "HTK" is a synonym for EphB4. Further, the datasheet states that the antibody is provided in a kit comprising a composition comprising the pharmaceutically acceptable carrier PBS. Inada et al teaches monoclonal (see Figure 2, page 2760) and polyclonal antibodies which bind to an extracellular domain of an EphB4 protein (page 2758, in particular), which this early reference refers to as HTK. One of skill in the art would recognize that purification of the antibodies would have involved producing a composition comprising the antibodies and a pharmaceutically acceptable carrier. One of skill in the art would further recognize that the antibodies taught by Stephenson et al or Inada et al would inherently inhibit activities of EphB4. At the very least, the polyclonal and monoclonal antibodies taught by Stephenson et al and Inada et al would

inhibit phosphorylation of EphB4 residues which they bind. Further, the polyclonal antibodies taught by Stephenson et al and Inada et al, and likely the monoclonal antibodies taught by Inada et al, would sterically inhibit the association between EphB4 and any of its binding partners, including Ephrin B2. An association between the extracellular domains of EphB4 and Ephrin B2 is disclosed in the specification on page 20 (page 20 lines 5-23, in particular). The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the antibodies of the prior art do not possess the same characteristics as the claimed antibodies. In the absence of evidence to the contrary, the burden is on Applicant to prove that the claimed antibodies are different from those taught by the prior art and to establish patentable differences. See In re Best 562F .2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2nd 1992 (PTO Bd. Pat. App. & Int. 1989).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 26-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending Application No. 10/949,720. Although the conflicting claims are not identical, they are not patentably distinct from each other because the antibodies of claims 1-23 of 10/949,720 anticipate the genus of antibodies which bind to an extracellular domain of an EphB4 protein and inhibit an activity of Ephb4 in the pending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER